

# Impact of Genetic Testing and Family Health History Based Risk Counseling on Behavior Change and Cognitive Precursors for Type 2 Diabetes

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**Abstract** Family health history (FHH) in the context of risk assessment has been shown to positively impact risk perception and behavior change. The added value of genetic risk testing is less certain. The aim of this study was to determine the impact of Type 2 Diabetes (T2D) FHH and genetic risk counseling on behavior and its cognitive precursors. Subjects were non-diabetic patients randomized to counseling that included FHH +/- T2D genetic testing. Measurements included weight, BMI, fasting glucose at baseline and 12 months and behavioral and cognitive precursor (T2D risk perception and control over disease development) surveys at baseline, 3, and 12 months. 391 subjects enrolled of which 312 completed the study. Behavioral and clinical outcomes did not differ across FHH or genetic risk but cognitive precursors did. Higher FHH risk was associated with a stronger perceived T2D risk ( $p_{\text{Kendall}} < 0.001$ ) and with a perception of “serious” risk ( $p_{\text{Kendall}} < 0.001$ ). Genetic risk did not influence risk perception, but was correlated with an increase in perception of “serious” risk for moderate ( $p_{\text{Kendall}} = 0.04$ ) and average FHH risk subjects ( $p_{\text{Kendall}} = 0.01$ ), though not for the high FHH risk

group. Perceived control over T2D risk was high and not affected by FHH or genetic risk. FHH appears to have a strong impact on cognitive precursors of behavior change, suggesting it could be leveraged to enhance risk counseling, particularly when lifestyle change is desirable. Genetic risk was able to alter perceptions about the seriousness of T2D risk in those with moderate and average FHH risk, suggesting that FHH could be used to selectively identify individuals who may benefit from genetic risk testing.

**Keywords** Genetic testing · Risk stratification · Family history · Primary prevention

## Introduction

Risk assessment and counseling impact risk perception and behavior change, particularly if risk assessment is tailored to the individual. (Claassen et al. 2010; Diabetes Prevention Program Research et al. 2009; Edwards et al. 2000; Heideman et al. 2011; Knowler et al. 2002; Kreuter and Strecher 1996; Tuomilehto et al. 2001) In recent years there has been a growing interest in adding genetic testing to the risk assessment toolkit, but it is unclear whether such testing will have an impact on behavior change (Marteau et al. 2010). Two recent trials comparing type 2 diabetes (T2D) behavioral outcomes based on results of genetic risk testing showed no increase in weight loss or motivation to change behavior (Grant et al. 2013; Voils et al. 2015). In contrast, family health history (FHH), a well-established component of health risk assessments, is both highly predictive and efficacious in promoting risk-lowering behaviors. For example, the presence of a first degree relative (parent or child) with T2D increases an individual’s risk from an average of 3.2 % to 14.3 % in some populations and counselling on FHH risk increases the

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likelihood of initiating health behaviors aimed at T2D prevention. (Annis et al. 2005; Hariri et al. 2006; Pijl et al. 2009).

Given the lack of impact of genetic testing on behavior change, it is useful to consider the cognitive constructs underlying these null results so that genetic risk assessment interventions may be tailored to increase potential impact. Two of these constructs are the perception of disease risk and of control over disease risk.

There are numerous models supporting the importance of *personal risk perception* on behavior change (e.g. Health Belief Model, Precaution Adoption Model) and research clearly demonstrates this relationship. (Brewer et al. 2007; Floyd et al. 2000; McVay et al. 2015) In the case of FHH, studies show that those with stronger FHHs for a given disease have increased perception of disease risk (Avis et al. 1989; Hariri et al. 2006). So far the only study to evaluate the impact of genetic risk on risk perception for T2D to date, found no difference (Grant et al. 2013).

Given the non-modifiable nature of FHH and genetic risk, the *perception of personal control* over disease risk could play an important role in limiting behavior change. It has been argued that those with stronger FHH or genetic risk would feel less able to control their risk of T2D development and therefore would be less likely to attempt behavior change. This may also vary by individuals and be further affected by culture and education level among other factors. There is conflicting evidence around this theory (Marteau and Weinman 2006; Pijl et al. 2009) and little is known about what risk assessment and counseling *in combination with* education about lifestyle modification may have.

In this paper we report a secondary analysis of the “Effect of T2D genetic risk information on health behaviors and outcomes” trial (Cho et al. 2012), evaluating the impact of FHH and genetic risk on behavior change, perception of T2D risk, and perception of personal control over development of T2D. We also examine how FHH risk and genetic risk may interact to influence cognitive constructs underlying behavior change.

## Materials and Methods

In the parent study, interested primary care patients were randomized to one of two groups: 1) control group who received standard T2D risk assessment (SRA) during a risk counseling session and 2) intervention group who received the standard T2D risk assessment that incorporated genetic risk results (SRA + G) during a risk counseling session. Both arms underwent risk counseling with a provider who was already part of the clinic staff. There was a third arm which included a small number of subjects who were interested in participating in the study but did not wish to undergo genetic testing. These subjects were excluded from this analysis since they were deemed unlikely to respond to genetic risk information in

the same way as subjects willing to undergo genetic testing and constituted a very small part of the overall sample ( $n = 18$ ) (Fig. 1). The study was approved by the Duke University Health System Institutional Review Board and registered in ClinicalTrials.gov (NCT00849563).

## Participants, Setting, and Intervention

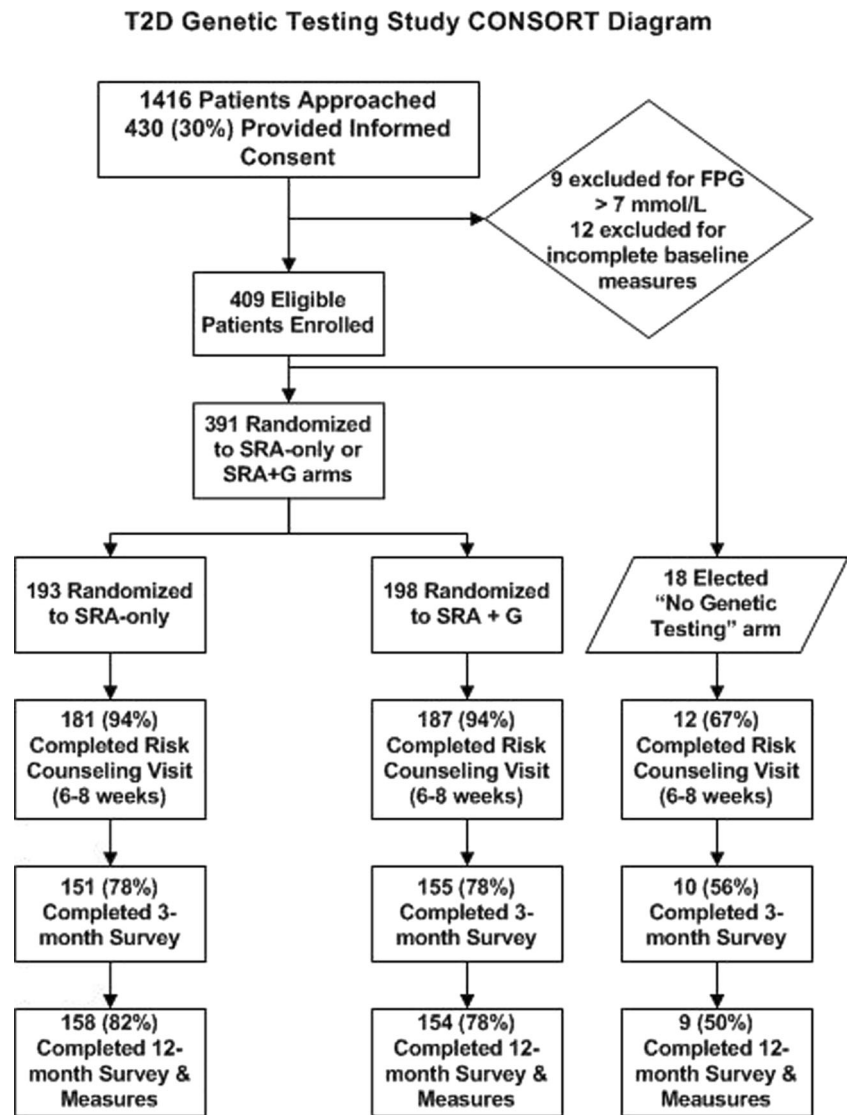
Full details of the protocol have previously been published (Cho et al. 2012). In brief, a convenience sample of patients awaiting fasting blood work was recruited from two primary care clinics in an academic healthcare system in North Carolina. Inclusion criteria included 1) age 18–81 years, 2) no self-reported history of diabetes, 3) no prior genetic testing for diabetes, and 4) not pregnant. Exclusion criteria included: 1) current or prior use of diabetic medications, 2) fasting blood glucose (FBG) level  $\geq 7$  mmol/L ( $\geq 126$  mg/dL) at enrollment, 3) non-fasting and unwilling to return for fasting bloodwork, and 4) unable to provide informed consent.

Consented participants completed baseline surveys, were weighed and measured, and had fasting blood work done. After 4–6 weeks, participants underwent a risk counseling session with a trained advanced practice provider where traditional risk factors were reviewed (BMI, FBG, race, ethnicity, FHH.) The intervention group also received their T2D genetic risk results during risk counseling. Risk counselling highlighted the modifiable nature of some risk factors and while allele results were explained as a non-modifiable component of risk, they were emphasized as not being absolute determinants of disease development. At 3 months, participants completed online psychosocial surveys. At 12 months, participants repeated clinical measurements and the same surveys.

## Measures and Outcomes

DNA testing was conducted with a CLIA-approved commercially available platform (deCode genetics, Chicago, IL.) for four single nucleotide polymorphisms (SNPs) at the *TCF7L2* (rs7903146) (OR 1.30–1.97,  $p$ -value  $< 0.001$  for impaired glucose tolerance), *CDKN2A/2B* (rs10811661) (OR 1.2–1.49,  $p$ -value  $< 0.001$ ), *CDKALI* (rs7756992) (OR 1.12,  $p$ -value = 0.007) and *PPARG* (rs1801282) (OR 1.14–1.25,  $p$ -value 0.002) genes (de Miguel-Yanes et al. 2011; Diabetes Genetics Initiative of Broad Institute of H, Mit, LU, et al. 2007; Scott et al. 2007; Tong et al. 2009). These were selected due to their established validity at the time of study initiation. Genetic test results were presented as the number of high risk alleles out of the 8 total alleles (2 per gene). Genetic risk was also categorized as average (0 alleles) or moderate ( $\geq 1$  allele). Given that all subjects were found to have at least one allele and were therefore in the moderate risk category, we did our analysis using

Fig. 1 CONSORT flow diagram



number of high risk alleles the subject had and not their genetic risk category. FHH risk was categorized as average, moderate, and high using the FHH risk model developed by Hariri and colleagues. (Table 1) (Hariri et al. 2006).

Psychosocial process measures of disease risk perception and perception of control over disease risk were assessed through surveys at baseline, 3 months, and 12 months (Table 2). Risk perception questions were designed specifically for this study based on the Common Sense Model principles (Leventhal et al. 1992; Marteau and Weinman 2006). Perceived control of T2D risk was measured using the personal control subscale of the Illness Perception Questionnaire (IPQ) (adapted for control over disease development) (Weinman et al. 1996). Scores were based on 1–5 scale responses to six questions.

In this analysis, the primary outcome is the impact of FHH risk level (for all participants) and genetic risk level (for intervention participants) on change in weight, BMI, FBG, and

physical activity level. Secondary outcomes include impact on the perception of 1) T2D risk, 2) personal control over T2D risk, and 3) seriousness of T2D risk. Analysis is restricted to those who have completed all stages of the study ( $n = 312$ ).

### Data Analysis

To ensure randomization occurred as expected, we analyzed the relationship between FHH risk category and study arm using Pearson's chi-square test, where a significant result indicates that two variables are not independent, and i.e. some relationship exists between them. The relationship between the number of risk alleles and 1) study arm and 2) FHH risk category was assessed using analysis of variance (ANOVA) F-test where a statistically significant result indicates that there is at least one pair of levels in the categorical variable which have significantly different effects on the numeric variable. To interrogate follow-up patterns in the survey responses at

**Table 1** Family health history risk categories

Risk category	Criteria
High risk	At least one of the following: <ul style="list-style-type: none"> <li>• Two first degree relatives with diabetes from the same lineage</li> <li>• One first and two second degree relatives with diabetes from the same lineage</li> <li>• Three second degree relatives with diabetes from the same lineage</li> </ul>
Moderate risk	Only: <ul style="list-style-type: none"> <li>• One first and one second degree relative with diabetes from the same lineage</li> <li>• One first degree relative with diabetes</li> <li>• Mother and father with diabetes</li> <li>• Two second degree relatives with diabetes from the same lineage</li> </ul>
Average risk	Only: <ul style="list-style-type: none"> <li>• One second degree relative with diabetes from one or both sides of the family</li> <li>• No family history of diabetes</li> </ul>

each time point, Pearson's chi-square was used to test relationship between participant follow-up and clinic site, gender, ethnicity, race, number of risk alleles, and FHH risk category. An ANOVA F-test was used to examine differences in participant follow-up by age and BMI.

The relationship between FHH risk category and primary outcome variables (BMI, weight, physical activity) was determined using an ANOVA F-test. To analyze the relationship between number of risk alleles and the primary outcomes, we used a linear regression model to determine if a statistically significant linear relationship exists between the variables.

To analyze the relationships of both FHH risk category and risk allele results with 1) perception of risk and 2) change in that risk over time, we used the Kendall's Tau rank correlation coefficient where a significant result indicates that a non-parametric directional relationship exists between the two

variables. We used an ANOVA F-test to analyze the relationship between FHH risk category and 1) IPQ score and 2) IPQ score change over time. To analyze the relationship between number of risk alleles and IPQ score, we used a linear regression model.

## Results

### Demographics

A total of 391 patients enrolled in the study (intervention  $N = 198$ , control  $N = 193$ ). Demographics are provided in Table 3. There was no significant difference in FHH risk category distribution between arms ( $p_{\text{Chisq}} = 0.25$ ). The mean number of risk alleles was 5 (SD 1.23, range 2–7) in the intervention arm and 4.8 (SD 1.3, range 1–8) in the control arm. For the total enrolled sample, FHH risk category and number of risk alleles did not show significant correlation. However when looking only at those who completed the entire study, a mostly white population (64%), FHH risk category did correlate with number of risk alleles (average FHH group had mean of 4.76 alleles; moderate FHH had 4.79 alleles; high FHH had 5.18 alleles,  $p_{\text{ANOVA}} = 0.018$ .)

### Follow-up Data Analysis

At 3 months, 86% ( $N = 170/198$ ) of intervention subjects and 88% ( $N = 169/193$ ) of controls completed requested surveys. At 12 months, 81% ( $N = 160/198$ ) of intervention subjects and 82% ( $N = 159/193$ ) of controls had completed the follow-up visit and surveys. Survey data at follow-up did not vary based on gender, study arm, FHH risk category, and number of risk alleles. Missing data for the 3 month follow-up varied by age, race, BMI and clinic location at follow-up. Subjects were less likely to have completed follow-up survey data if

**Table 2** Psychosocial survey questions

Risk perception	
• My risk for diabetes is serious:	Answer choices: Strongly disagree; disagree; not sure/don't know; agree; strongly agree
• What do you think is your chance of getting diabetes in your lifetime?	Answer choices: Scale of 1–5 (never will get diabetes to definitely will get diabetes)
Personal Control Illness Perception Questionnaire	
• There is a lot that I can do to control my risk for diabetes.	Answer choices for all questions: Strongly disagree – Disagree—Neither agree nor disagree— Agree—Strongly Agree (Scale of 1-5)
• What I do can determine whether or not I get diabetes.	
• Whether or not I get diabetes depends on me.	
• Nothing I can do will affect my risk for diabetes.*	
• I have the power to influence my risk for diabetes.	
• Nothing I can do will change my risk for diabetes.*	

\* Scores reversed when calculating score out of 30

**Table 3** Demographics by study arm

	SRA + G (N = 198)	SRA (N = 193)
Age [mean (sd)]	50.9 (12.8)	49.3 (13.6)
Male [N (%)]	62 (31.3 %)	57 (29.5 %)
BMI [mean (sd)]	30.6 (7.1)	30.9 (7.4)
FBG [mean (sd)]	94.6 (10.5)	95.3 (10.7)
Race [N (%)]		
White	114 (57.6 %)	117 (60.9 %)
Black	60 (30.3 %)	51 (26.6 %)
Asian	10 (5.0 %)	9 (4.7 %)
American Indian/Alaskan	2 (1.0 %)	2 (1.0 %)
Native Hawaiian	0	2 (1.0 %)
Mixed racial	11 (5.6 %)	9 (4.7 %)
Not reported	1 (0.5 %)	2 (1.0 %)
FHH [N]		
Average	78	87
Moderate	59	45
High	61	61
Genetic alleles [mean, (sd)]	5 (1.23)	4.8 (1.3)

they had higher BMI (34.9 vs. 30.1,  $p_{ANOVA} < 0.001$ ), were of younger age (42.4 vs. 51.2,  $p_{ANOVA} < 0.001$ ), were black (25.2 % vs. 8.7 % of whites,  $p_{Chisq} < 0.001$ ), and were seen at the clinic with a lower SES patient population (20.0 % missing vs. 7.6 % missing,  $p_{Chisq} < 0.001$ ). These differences persisted at 12 months (BMI 34.6 vs 29.9; age 41.7 years vs 51.9 years; blacks 33.3 % vs. whites 11.2 %; 27.2 % of lower SES clinic vs 10.9 % higher SES clinic,  $p < 0.001$  for all variables.)

### Health Behavior

For the overall study population, there were no significant changes in the primary outcomes (BMI, weight, level of physical activity, FBG) from baseline to post-counseling time point of 12 months. In addition, neither FHH nor genetic risk levels affected changes in weight, BMI, FBG or level of physical activity from baseline to post-counseling.

### Risk Perception

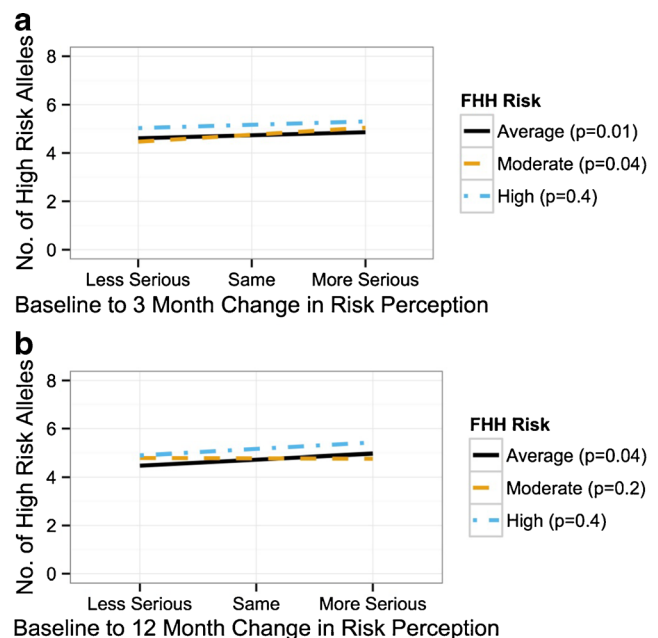
#### *My Risk for Diabetes is Serious*

Over half the participants (53.2 %,  $N = 165/310$ ) agreed or strongly agreed that their risk of diabetes was serious at baseline. This perception persisted over the course of the study with 64.9 % ( $N = 202/311$ ) agreeing at 12 month follow-up. This perception correlated with FHH risk across time points (all  $p_{Kendall's} < 0.001$ ) and did not change significantly from baseline to post-risk counseling session at 3 months and

12 months based on FHH risk. Within the SRA + G arm, those with more risk alleles were more likely to have a positive change in their response from baseline to 3 months ( $p_{Kendall's} < 0.001$ ) and to 12 months ( $p_{Kendall's} = 0.03$ ). However, this relationship between number of risk alleles and change in risk perception was strongest in SRA + G participants with average FHH with a positive change at 3 months ( $p_{Kendall's} = 0.01$ ) and 12 months ( $p_{Kendall's} = 0.04$ ). For those with moderate FHH risk, the number of risk alleles was associated with a positive change at 3 months ( $p_{Kendall's} = 0.04$ ) but not at 12 months. For those with high FHH risk, risk allele count was not associated with a statistically significant change in perception of risk seriousness at 3 months or 12 months. (Fig. 2).

### What Is your Chance of Getting Diabetes in your Lifetime?

Responses did not vary based on study arm (Table 4). FHH risk level correlated with responses across time points ( $p_{Kendall's} < 0.001$ ). Following the risk counseling session, there was no significant change in score from baseline to 3 months or to 12 months. In regards to risk alleles, there was no correlation between number of risk alleles and change in score from baseline to 3 months or 12 months. This remained true for each FHH risk group independently as well; risk alleles had did not appear to have an impact on response within specific FHH risk groups.



**Fig. 2** Linear regression trend lines describing the relationship between change in perception of seriousness of risk between baseline and 3 month responses (a) or baseline and 12 month responses (b) and the number of high risk alleles, color code by FHH risk with Kendall Rank correlation  $p$ -values shown

**Table 4** Your chance of getting T2D in your lifetime

	Overall <i>N</i> = 312 (%)	Average FHH <i>N</i> = 137 (%)	Moderate FHH <i>N</i> = 82 (%)	High FHH <i>N</i> = 93 (%)	Average allele (SD) in SRA + GT
Baseline*					
1 <sup>†</sup>	42 (13.46)	32 (23.36)	7 (8.54)	3 (3.23)	4.84 (1.21)
2	71 (22.76)	37 (27.01)	20 (24.39)	14 (15.05)	5.16 (1.30)
3	130 (41.67)	47 (34.31)	38 (46.34)	45 (48.39)	4.93 (1.28)
4	57 (18.27)	18 (13.14)	15 (18.29)	24 (25.81)	4.85 (1.05)
5	12 (3.85)	3 (2.19)	2 (2.44)	7 (7.53)	5.80 (0.45)
3 months <sup>‡</sup>					
1	19 (6.09)	16 (11.68)	2 (2.44)	1 (1.08)	5.14 (1.07)
2	81 (25.96)	46 (33.58)	22 (26.83)	13 (13.98)	5.00 (1.33)
3	162 (51.92)	63 (45.99)	47 (57.32)	52 (55.91)	4.84 (1.16)
4	41 (13.14)	8 (5.84)	10 (12.2)	23 (24.73)	5.38 (1.28)
5	9 (2.89)	4 (2.92)	1 (1.22)	4 (4.30)	5.50 (1.29)
12 months <sup>¥</sup>					
1	47 (15.00)	36 (26.28)	6 (7.32)	5 (5.44)	4.67 (1.46)
2	100 (32.00)	47 (34.31)	28 (34.15)	25 (27.17)	4.76 (1.24)
3	106 (34.00)	43 (31.39)	32 (39.02)	31 (33.70)	5.18 (1.13)
4	43 (14.00)	8 (5.84)	14 (17.07)	21 (22.83)	5.29 (1.10)
5	15 (4.80)	3 (2.19)	2 (2.44)	10 (10.87)	5.38 (1.06)

<sup>†</sup> 1 = Definitely will NOT get T2D, 5 = Definitely will get T2D

\*Kendall's Tau for FHH analysis = 0.27, *p*-value < 0.001; ANOVA *p*-value for allele analysis = 0.45

<sup>‡</sup> Kendall's Tau for FHH analysis = 0.29, *p*-value < 0.001; ANOVA *p*-value for allele analysis = 0.39

<sup>¥</sup> High FHH group at 12 month =92; Kendall's Tau for FHH analysis = 0.29, *p*-value < 0.001; ANOVA *p*-value for allele analysis = 0.16

## Perception of Control

Overall at baseline there was a strong perception of personal control over T2D risk (mean 24.08, SD 3.43) that did not vary based on FHH risk category or number of risk alleles. Scores also did not change significantly from baseline to 3 months or 12 months for the group overall or based on FHH or genetic risk. We also examined for impact of perception of personal control on primary behavioral outcomes described above. Perception of control scores did not appear to have a significant impact on these behaviors.

## Discussion

While there was no change observed in behavior based on receipt of FHH or genetic risk level, there are several lessons learned through this study. Patients' understanding of their own risk is a key first step in the process of behavior change (Brewer et al. 2007; Codori et al. 2001; Murabito et al. 2001). Therefore, understanding what affects patients' perceptions of their risk and how to deliver that information is essential. This study demonstrates that subjects have a strong understanding of the role of FHH in their disease risk and perceive their risk as more serious if they have higher FHH risk. The same was

not true for genetic risk. Being informed about personal genetic risk did not strongly affect subjects' perception of disease risk, but it did influence perception of the seriousness of their risk. Interestingly this effect varied based on the subject's FHH risk. Perceptions of those with the highest FHH risk were not affected by risk allele status. It was only among those with average or moderate FHH risk that genetic test results influenced their perceptions of seriousness. The fact that FHH risk correlated with genetic allele status and that those with high FHH already saw their risk as serious likely contributes to this observation. Risk allele status could do little to attenuate their already strong response. On average those with lower FHH risk did not see their risk as being as serious at baseline and thus knowledge of higher risk allele status could influence perceptions. The observed difference in impact of risk alleles on perception by FHH risk is worth considering when determining who to test, if genetic testing for disease risk were to become more commonplace.

Reassuringly, subjects showed strong perceptions of control over disease risk regardless of their FHH or genetic risk level. This also was something that was not impacted significantly by the risk counseling sessions. There appears to be a great deal of common knowledge about the power of lifestyle change to affect disease development allowing subjects to feel they have control over their risk of T2D development.

Lack of impact on behavior change may be attributed to several factors. Previous studies have shown that risk counseling can impact behavior change (Claassen et al. 2010; Diabetes Prevention Program Research et al. 2009; Edwards et al. 2000; Heideman et al. 2011; Knowler et al. 2002; Kreuter and Strecher 1996; Tuomilehto et al. 2001). But as with all behavior change, frequent and repetitive interventions are more likely to succeed (Knowler et al. 2002; Soler et al. 2010; Tuomilehto et al. 2001). This study was designed as a one-time intervention to evaluate the impact of adding risk allele results to standard risk counseling. The one-time nature of the intervention may not have been the ideal when seeking sustained behavior modification. In addition, currently known genetic variants associated with diabetes do not have a large impact on overall risk. Subjects may have recognized the weakness of this association during risk counselling sessions and therefore not felt significantly motivated to change behavior. With the discovery of stronger genetic associations, impact of genetic testing on behavior change may be found more promising.

### Study Limitations

There are significant limitations to this study that should be addressed. This is a secondary subgroup analysis. In addition, there may have been unintended variability in the risk assessment sessions depending on risk factor results. Since these sessions were conducted by someone within the clinic who by nature of the intervention could not be blinded to study arm or subjects' risk level, it is possible that the counselor could have put more or less emphasis on the importance of lifestyle change and ability to control disease progression with those at higher FHH or genetic risk. Additionally while subjects were counselled about their genetic risk, their understanding of that information was not assessed. If subjects had a faulty understanding of the information, this could affect their psychosocial responses and potentially their behavior.

In regard to measurement limitations, the risk perception questions were designed specifically for this study and were not from a validated survey. A strong theoretical model (i.e. Common Sense model) (Leventhal et al. 1992) was used in designing the questions; however, they were not validated prior to use in the study. While the perception of control questions were from a validated survey, the IPQ (Weinman et al. 1996), the questions were modified slightly to address control over disease *development* instead of disease *progression*, which the IPQ was originally designed to test.

In regard to generalizability, minorities and subjects that were younger or more obese were less likely to complete the study. Therefore, conclusions cannot be as confidently drawn about these populations and targeted interventions for these groups should be considered. Interestingly FHH risk for the initial study population did not correlate with number of risk alleles although the largely white subset that completed the

study did show association between FHH risk and number of risk alleles. This is not unexpected since the association of these mutations with development of T2D has been validated in primarily white populations (Cornelis et al. 2009; Tong et al. 2009). Further research in other racial and ethnic populations is necessary in order to determine which genetic variants must be considered in non-white populations.

### Research Recommendations and Practice Implications

Conveyance of genetic risk may augment FHH within certain groups. As evidence for the accuracy of genetic testing in risk prediction grows, specific thought and research efforts should be focused upon who should get testing (those already at highest risk or those at more moderate risk whose risk may change as a result of testing) and how best to deliver that information. In addition, further efforts should be made to understand how risk assessment interventions, perhaps with ongoing counseling and coaching, can affect behavior change and ultimately prevent disease development.

In 2015, FHH is still the most predictive and influential genetic test we have available. In this study we saw that patients have a strong inherent understanding of the importance of FHH to their personal risk. More work needs to be done to understand how FHH risk and patients' experience with their own family's disease processes can be used to activate patients for behavior change and risk mitigation (Codori et al. 2001). Medical providers should seek to understand their patients' family history and take advantage of their intrinsic risk perception to guide counseling efforts towards lifestyle modification and disease prevention. This should be done through frequent and personalized reminders of what the individual patient's risks are and how they can address them through specific changes to behavior.

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### Compliance with Ethical Standards

**Conflict of Interest** R. Ryanne Wu, Rachel A. Myers, Elizabeth R. Hauser, Allison Vorderstrasse, Alex Cho, Geoffrey S. Ginsburg and Lori A. Orlando declare they have no conflicts of interest.

**Human Studies and Informed Consent** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

**Animal Studies** No animal studies were carried out by the authors for this article.

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